

1. A method of inhibiting alpha synuclein (aS) mediated toxicity, the method comprising contacting a cell expressing aS with a composition comprising an amount of a compound effective to inhibit aS mediated toxicity in the cell, wherein the compound is selected from the group consisting of nordihydroguaiaretic acid, ibuprofen, D,L-a-  
5 hydroxy-butyric acid, m-cresol, hexachlorophene, ruthenium red, sodium metasilicate, sodium metavanadate, sodium cyanide, and tetracycline.

2. A method of inhibiting aS mediated toxicity, the method comprising contacting a cell expressing aS with a composition comprising an amount of a compound  
10 effective to inhibit aS mediated toxicity in the cell, wherein the compound is selected from the group consisting of a fungicide, lipoxygenase inhibitor, prostaglandin synthetase inhibitor, membrane detergent, electron transporter, mitochondrial Ca<sup>++</sup> porter, toxic anion, and antibiotic.

15 3. A method of inhibiting aS mediated fibril formation, the method comprising contacting a cell expressing aS with a composition comprising an amount of a compound effective to inhibit aS mediated fibril formation in the cell, wherein the compound is selected from the group consisting of nordihydroguaiaretic acid, ibuprofen, D,L-a-  
hydroxy-butyric acid, m-cresol, hexachlorophene, ruthenium red, sodium metasilicate,  
20 sodium metavanadate, sodium cyanide, and tetracycline.

4. A method of inhibiting aS mediated fibril formation, the method comprising contacting a cell expressing aS with a composition comprising an amount of a compound effective to inhibit aS mediated fibril formation in the cell, wherein the compound is  
25 selected from the group consisting of a fungicide, lipoxygenase inhibitor, prostaglandin synthetase inhibitor, membrane detergent, electron transporter, mitochondrial Ca<sup>++</sup> porter, toxic anion, and antibiotic.

5. A method of treating or preventing Parkinson's disease, the method  
30 comprising administering to an individual in need thereof a pharmaceutical composition comprising a therapeutically effective amount of a compound selected from the group

consisting of nordihydroguaiaretic acid, ibuprofen, D,L-a-hydroxy-butyric acid, m-cresol, hexachlorophene, ruthenium red, sodium metasilicate, sodium metavanadate, sodium cyanide, and tetracycline.

5           6. A method of treating or preventing Parkinson's disease, the method comprising administering to an individual in need thereof a pharmaceutical composition comprising a therapeutically effective amount of a compound selected from the group consisting of a fungicide, lipoxygenase inhibitor, prostaglandin synthetase inhibitor, membrane detergent, electron transporter, mitochondrial  $\text{Ca}^{++}$  porter, toxic anion, and  
10       antibiotic.

          7. A method of inhibiting huntingtin (htt) mediated toxicity, the method comprising contacting a cell expressing htt with a composition comprising an amount of a compound effective to inhibit htt mediated toxicity in the cell, wherein the compound is  
15       selected from the group consisting of a clioquinol, histidine-containing dipeptide, nordihydroguaiaretic acid, m-cresol, and guanidine hydrochloride.

          8. The method of claim 7, wherein the compound is a clioquinol selected from the group consisting of 8-Hydroxyquinoline, 5,7-Dichloro-8-hydroxy-quinaldine, and 8-  
20       Hydroxy-5-nitroquinoline.

          9. A method of inhibiting htt mediated toxicity, the method comprising contacting a cell expressing htt with a composition comprising an amount of a compound effective to inhibit htt mediated toxicity in the cell, wherein the compound is selected  
25       from the group consisting of a chelator, fungicide, lipoxygenase inhibitor, membrane detergent, and chaotropic agent.

          10. A method of inhibiting htt mediated fibril formation, the method comprising contacting a cell expressing htt with a composition comprising an amount of a compound  
30       effective to inhibit htt mediated fibril formation in the cell, wherein the compound is

selected from the group consisting of a clioquinol, histidine-containing dipeptide, nordihydroguaiaretic acid, m-Cresol, and guanidine hydrochloride.

11. The method of claim 10, wherein the compound is a clioquinol selected from  
5 the group consisting of 8-Hydroxyquinoline, 5,7-Dichloro-8-hydroxy-quinaldine, and 8-Hydroxy-5-nitroquinoline.

12. A method of inhibiting htt mediated fibril formation, the method comprising  
10 contacting a cell expressing htt with a composition comprising an amount of a compound effective to inhibit htt mediated fibril formation in the cell, wherein the compound is selected from the group consisting of a chelator, fungicide, lipoxygenase inhibitor, membrane detergent, and chaotropic agent.

13. A method of treating or preventing Huntington's disease, the method  
15 comprising administering to an individual in need thereof a pharmaceutical composition comprising a therapeutically effective amount of a compound selected from the group consisting of a clioquinol, histidine-containing dipeptide, nordihydroguaiaretic acid, m-Cresol, and guanidine hydrochloride.

20 14. The method of claim 13, wherein the compound is a clioquinol selected from the group consisting of 8-Hydroxyquinoline, 5,7-Dichloro-8-hydroxy-quinaldine, and 8-Hydroxy-5-nitroquinoline.

25 15. A method of treating or preventing Huntington's disease, the method comprising administering to an individual in need thereof a pharmaceutical composition comprising a therapeutically effective amount of a compound selected from the group consisting of a chelator, fungicide, lipoxygenase inhibitor, membrane detergent, and chaotropic agent.

30 16. A method of identifying a compound that inhibits aS mediated toxicity, the method comprising:

providing a yeast cell expressing an amount of aS that reduces viability of the cell;

contacting the cell with candidate agent selected from the group consisting of a fungicide, lipoxygenase inhibitor, prostaglandin synthetase inhibitor, membrane  
5 detergent, electron transporter, mitochondrial  $\text{Ca}^{++}$  porter, toxic anion, and antibiotic; and

determining whether the candidate agent enhances viability of the cell, to thereby identify a compound that inhibits aS mediated toxicity.

10 17. A method of identifying a compound that inhibits htt mediated toxicity, the method comprising:

providing a yeast cell expressing an amount of htt that reduces viability of the cell;

contacting the cell with a candidate agent selected from the group consisting of a  
15 chelator, fungicide, lipoxygenase inhibitor, membrane detergent, and chaotropic agent; and

determining whether the candidate agent enhances viability of the cell, to thereby identify a compound that inhibits htt mediated toxicity.

20 18. A method of identifying a compound that inhibits htt mediated toxicity, the method comprising:

providing a yeast cell expressing an amount of htt that reduces viability of the cell;

contacting the cell with a clioquinol; and

25 determining whether the clioquinol enhances viability of the cell, to thereby identify a compound that inhibits htt mediated toxicity.

19. A method of identifying a compound that inhibits aS mediated toxicity, the method comprising:

30 identifying a candidate agent that stimulates the expression or activity of a protein encoded by a gene selected from the group consisting of CHD5, CPT2, CTH, AMPD2,

AMPD1, CHD1L, NIT1, ACOX2, NIT2, ENPP6, SMARCA5, ENPEP, SMARCAD1, ACOX3, ARTS-1, LNPEP, LRAP, CHD1, SOD2, HBS1L, ENPP3, ENPP1, EEF1A1, ENPP5, CROT, UBE2H, RAD54B, CRAT, SMARCA2, CHAT, ERCC6, HELLS, SUPV3L1, BTAF1, AMPD3, CPT1A, EP400, TRHDE, CHD4, ATP7B, CHD2, ANPEP, KIAA1259, HAGH, GSPT1, SRCAP, FLJ12178, ACQX1, NPEPPS, PEMT, CPT1C, SMARCA4, EEF1A2, ARFRP1, CHD6, CPT1B, GSPT2, ATP7A, and SMARCA1;

contacting a cell expressing aS with the candidate agent; and

determining whether the candidate agent enhances viability of the cell, to thereby identify a compound that inhibits aS mediated toxicity.

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20. A method of identifying a compound that inhibits aS mediated toxicity, the method comprising:

providing a cell expressing aS and not expressing a wild type gene selected from the group consisting of CHD5, CPT2, CTH, AMPD2, AMPD1, CHD1L, NIT1, ACOX2, NIT2, ENPP6, SMARCA5, ENPEP, SMARCAD1, ACOX3, ARTS-1, LNPEP, LRAP, CHD1, SOD2, HBS1L, ENPP3, ENPP1, EEF1A1, ENPP5, CROT, UBE2H, RAD54B, CRAT, SMARCA2, CHAT, ERCC6, HELLS, SUPV3L1, BTAF1, AMPD3, CPT1A, EP400, TRHDE, CHD4, ATP7B, CHD2, ANPEP, KIAA1259, HAGH, GSPT1, SRCAP, FLJ12178, ACQX1, NPEPPS, PEMT, CPT1C, SMARCA4, EEF1A2, ARFRP1, CHD6, CPT1B, GSPT2, ATP7A, and SMARCA1, such that the cell has reduced viability as compared to a cell not expressing aS and expressing the wild type gene;

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contacting the cell with a candidate agent; and

determining whether the candidate agent enhances viability of the cell, to thereby identify a compound that inhibits aS mediated toxicity.

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21. A method of identifying a compound that inhibits aS mediated toxicity, the method comprising:

identifying a candidate agent that modulates osmotic sensitivity or the activity of detergents, oxidants, or drugs affecting transport;

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contacting a yeast cell expressing aS with the candidate agent; and

determining whether the candidate agent enhances viability of the cell, to thereby identify a compound that inhibits aS mediated toxicity.